



Hopkins Hatzopoulos, M., Eastoe, J., Dowding, P. J., Grillo, I., Demé, B., Rogers, S. E., Heenan, R., & Dyer, R. (2012). Effects of structure variation on solution properties of hydrotropes: Phenyl versus cyclohexyl chain tips. *Langmuir*, 28(25), 9332-9340.
<https://doi.org/10.1021/la301222m>

Peer reviewed version

License (if available):
CC BY-NC

Link to published version (if available):
[10.1021/la301222m](https://doi.org/10.1021/la301222m)

[Link to publication record in Explore Bristol Research](#)
PDF-document

This is the author accepted manuscript (AAM). The final published version (version of record) is available online via ACS at <http://pubs.acs.org/doi/abs/10.1021/la301222m>. Please refer to any applicable terms of use of the publisher.

University of Bristol - Explore Bristol Research

General rights

This document is made available in accordance with publisher policies. Please cite only the published version using the reference above. Full terms of use are available:
<http://www.bristol.ac.uk/red/research-policy/pure/user-guides/ebr-terms/>

Effects of structure variation on solution properties of hydrotropes: phenyl versus cyclohexyl chain tips

Marios Hopkins Hatzopoulos¹

Julian Eastoe^{*1}

Peter J. Dowding²

Isabelle Grillo³

Bruno Demé³

Sarah E. Rogers⁴

Richard Heenan⁴

Robert Dyer⁵

1. School of Chemistry, University of Bristol, Cantock's Close, Bristol, BS8 1TS, UK

2. Infineum UK Ltd., Milton Hill Business & Technology Centre, Abingdon, Oxfordshire OX13 6BB, UK

3. ILL, BP 156-X, F-38042 Grenoble Cedex, France

4. ISIS-STFC, Rutherford Appleton Laboratory, Chilton, Oxon OX11 0QX, UK

5. Krüss UK, School of Chemistry, University of Bristol, Cantock's Close, Bristol, BS8 1TS, UK

* Corresponding author

Abstract

The physicochemical behaviour of the phenyl-*n*-alkanoate (PhenCx) and cyclohexyl-*n*-alkanoate (CyclohexCx) series has been investigated, supporting previous work on the understanding of hydrotropes (Hopkins Hatzopoulos, M., Eastoe J., Dowding P.J., Rogers S.E., Heenan, R., Dyer, R., *Langmuir*, **2011**, 27, 12346-12353). Electrical conductivity, surface tension, ^1H NMR and small-angle neutron scattering (SANS) were used to study adsorption and aggregation in terms of critical aggregation concentration (*cac*). The PhenCx series exhibited very similar $d\log(cac) / dn$ to *n*-alkylbenzoates (CnBenz), exhibiting two branches of behaviour, with a common inflection point at four linear carbons, whereas the CyclohexCx series showed no break point. Electrical conductivity and ^1H NMR concentration scans indicate a difference in physicochemical behaviour between higher and lower homologues in both the PhenCx and CyclohexCx series. Surface tension measurements with compounds belonging to either group gave typical Gibbs adsorption profiles, having $d\log(cac) / dn$ curves consistent with limiting head group areas in the region of (35-55 Å²) indicating monolayer formation. Small-angle neutron scattering (SANS) profiles showed no evidence for aggregates below the electrical conductivity determined *cac* values, inferring an 'on-off' mode of aggregation. Analyses of SANS profiles was consistent with charged ellipsoidal aggregates, persisting from lower through to higher homologues in both the PhenCx and CyclohexCx series.

Introduction

The physicochemical behaviour of short chain organic salts has been the issue of much debate, but of little scientific research in comparison to common surfactants. An array of these organic salts, commonly known as hydrotropes, has been observed to facilitate increased solubilisation of insoluble organic compounds above a salt specific concentration. The broad class of hydrotropes encompasses a wide variety of types (anionic, cationic, neutral) and molecular structures, which has hampered any general overview of behaviour. The point of contention has always been the mechanism of hydrotrope action, and how they impart increased solubility of hydrophobic compounds. The formation of complexes between solute and hydrotrope [1], and action as structure makers or breakers [2] have been speculated before. On the other hand, association or aggregation of hydrotropes has been supported by a number of studies [3-5], being conclusively demonstrated by small-angle neutron scattering (SANS) experiments on common ionic hydrotropes [6]. Having shown that hydrotropes aggregate the mechanism of association is under debate. A gradual change in physicochemical properties is normally observed (e.g. electrical conductivity, dye solubilisation) [3-5], leading to the view that hydrotropes associate in a stepwise manner, rather than the 'on-off' mechanism which is characteristic of surfactants. This is considered as a distinguishing feature of hydrotropes compared with classical surfactants. Balasubramanian and Srinivas [7] proposed a distinction between hydrotropes and surfactants after examining an homologous series of *n*-alkylbenzenesulfonates to find where hydrotropes 'become' surfactants: a clear point of departure could not be identified. Recently, Hatzopoulos et al. [8] studied aqueous solutions of the sodium *n*-alkylbenzoate (C_nBenz) series employing a range of techniques. Classical methods such as electrical conductivity and ¹H NMR concentration scans showed that lower homologues exhibit gradual changes in behaviour, generally observed previously for hydrotropes. However, when the alkyl tail consisted of four or more methylene (CH₂) groups, behaviour characteristic of surfactants was observed. Surface tension measurements on the other hand produced typical Gibbs adsorption profiles throughout the homologous series, implying no distinction between the behaviour for higher homologues and the lower 'hydrotropic' members of the series. SANS data also concurred with this, all recorded profiles being consistent with charged ellipsoidal aggregates, suggesting

that 'hydrotropes' do not differ in their overall physicochemical properties to common surfactants. Scattering profiles also indicated that no aggregates formed below the *cac*, again characteristic of an 'on-off' type of transition from a chaotic solution to an aggregate dispersion. A further point was that for such compounds not all carbon atoms in the molecule are thermodynamically equivalent, though still hydrophobic enough to drive aggregation.

This work extends that of [8] shedding more light on these systems. It aims to probe the additive nature of hydrophobicity by investigating an analogous series of alkylbenzoates, being phenyl-*n*-alkanoates (PhenCx) or cyclohexyl-*n*-alkanoates (CyclohexCx). The generic structures are shown inset in Figure 1, where *x* is the number of linear carbons including the headgroup carbon. This structural switch reveals the change from cyclic aromatic to cyclic aliphatic chain tips, to explore the distinction between these different but related groups. Common commercial surfactants, like those from the Triton series, can be found in aromatic and reduced cyclohexyl forms; therefore it is of interest to isolate the effects of this general structural switch on physicochemical behaviour. The phenyl ring is planar, and at 25 °C the cyclohexyl ring predominantly adopts a chair conformation [9]. Even though these two groups (phenyl vs cyclohexyl) differ by a mere five H atoms, as seen below there are some quite surprising effects on solution properties.

Experimental

Materials. All chemicals were purchased from Sigma Aldrich at the highest purity available. The sodium phenyl-*n*-alkanoates and cyclohexyl-*n*-alkanoates were synthesized from the parent acids. Sodium hydroxide was purchased from Fischer Scientific (97%). D₂O for NMR and SANS experiments was purchased from Aldrich (99.9%). EDTA tetrasodium salt, used in surface tension experiments was also purchased from Aldrich (99.5%). Activated carbon was purchased from Lancaster and used as received.

Methods. Compounds were prepared according to [8]. Sodium salts were generated by refluxing equimolar amounts of acid and NaOH for 8 hours, in approximately 1.5 times the minimum amount of ethanol required to dissolve the acid. The hot solutions were passed over carbon black and the collected filtrate was allowed to boil whilst distilling excess ethanol. The solutions were then allowed to cool; the products were collected by filtration and washed with cold ethanol. The products were then dissolved in deionised water, and any excess acid was extracted by shaking with distilled diethyl ether, then the products were collected by evaporation of the aqueous phase. The powders were placed in a vacuum-oven at 40 °C for 24 hrs over refreshed phosphorus pentoxide.

Electrical conductivities were determined using a Jenway Model 4510 Conductivity/TDS meter with temperature controlled at 25 ± 0.1 °C (thermostatic water bath).

NMR proton shifts were measured using a Varian 400MHz instrument at 25 °C, relative to HDO at 4.75 ppm.

Surface tension measurements were measured using the Wilhelmy plate method with a Krüss K100 instrument at 25 °C. Protocols for purification of the amphiphilic

salts are given in Supporting Information. Solutions were prepared with the necessary minimum amount of the chelating agent EDTA to sequester divalent ions introduced as impurities by NaOH in the preparation of the sodium salts (Supporting Information). All glassware was prewashed with 50% nitric acid and thoroughly rinsed with deionised water. The platinum plate was held over a blue flame until red hot after every measurement, and then cooled to room temperature before every use.

Small-Angle Neutron Scattering (SANS) was carried out on the D16 instrument at the Institute Laue Langevin (ILL). The wavelength at take off was 4.752 Å. A sample to detector distance of 900 mm was employed using three detector angles at 12°, 28° and 44°, giving rise to a Q range of 0.01-1.2 Å⁻¹. The sample changer was set at a 21° angle. The slits 1 were fully open at horizontally 15 mm and vertically 136 mm, whereas slits 2 (closest to the sample) were set at 5 mm horizontally and 8.8 mm vertically.

Additional measurements were made on the SANS2d instrument at ISIS at the Rutherford Laboratory. A simultaneous Q-range of 0.0045 - 0.75 Å⁻¹ on the SANS2d instrument was achieved utilizing an incident wavelength range of 1.75 - 16.5 Å and employing an instrument set up of L1 = L2 = 4 m, with the 1 M2 detector offset vertically 150 mm and sideways 180 mm. The PhenCx series was measured on D16, as were CyclohexC1 and CyclohexC5. The compounds CyclohexC2-4 were measured on SANS2d.

The momentum transfer Q is defined as:

$$Q = \frac{4\pi \sin(\theta/2)}{\lambda} \quad 1$$

where θ is the scattering angle and λ is the incident neutron wavelength.

D₂O was used to prepare the solutions, providing the necessary contrast. Samples were contained in 2 mm path length Hellma fused silica cells. The SANS data were

normalised for transmission and subtraction of the empty cell and solvent background.

The FISH program was employed for data modelling [10]. The scattering profile curve is broadly described by:

$$I(Q) \propto P(Q)S(Q) \quad 2$$

where $P(Q)$ is the form factor, which contains information about the size and shape of the aggregates, and $S(Q)$ is the structure factor reporting on interactions. Here the ellipsoidal $P(Q)$ model was used in final fits, in combination with a Hayter-Penfold charge repulsion $S(Q)$ [11]. The ellipsoid aspect ratio X is characterised by two principal radii R_1 and R_3 :

$$X = R_3/R_1 \quad 3$$

Other model parameters include the volume fraction ϕ , the Debye length κ^{-1} and the effective radius of the charged micelle $R_{S(Q)}$. An approximate value of κ^{-1} value can be calculated by:

$$\kappa = \left(\frac{2F^2 \rho I}{\epsilon_0 \epsilon_r RT} \right)^{\frac{1}{2}} \quad 4$$

F is the Faraday constant, ρ is the solvent density, I is the ionic strength, ϵ_0 is the permittivity of free space and ϵ_r is the solvent dielectric constant, R is the gas constant and T the temperature.

The first approaches to fitting used hydrophobic tail lengths calculated using the Tanford equation [12] (eq.5)

$$l_{max} = 1.5 + 1.265n \quad 5$$

where l_{max} is the fully extended chain and n is the carbon number of the linear chain. It was assumed that a benzene ring ~ 3.5 CH₂ in length [13]. The micellar radii R_1 , and R_3 were minimized in the final analyses.

Results and Discussion

Electrical Conductivity. Electrical conductivity was employed as a first estimation of the *cacs* and the values are shown in Table 1. Comparing the *cac* values of compounds containing the same number of carbons it is readily appreciated that the higher homologues ($x = 4, 5$) of the saturated compounds have significantly lower *cac* values to the corresponding aromatic. The opposite trend however is noted when comparing the lower homologues ($x = 1 - 3$). In both classes of compounds the conductivity profiles showed a slightly curved behaviour for the lower homologues, whilst the higher ones exhibited a clear break, which is readily identifiable as a critical point and is associated with reaching the *cmc* of common surfactants. Figure 1 presents two example cases of each category, illustrating examples of readily identifiable changes in behaviour as a function of concentration in the higher homologue, but instead a gradual change in slope in the lower homologues.

Table 1. Critical aggregation concentration (*cac*) values as determined by electrical conductivity

<i>cac</i> / M		
Carbon number	PhenCx	CyclohexCx
6	0.17	-
5	0.31	0.08
4	0.37	0.18
3	0.39	0.28
2	-	0.60
1	0.48*	0.97

* Data from [8]

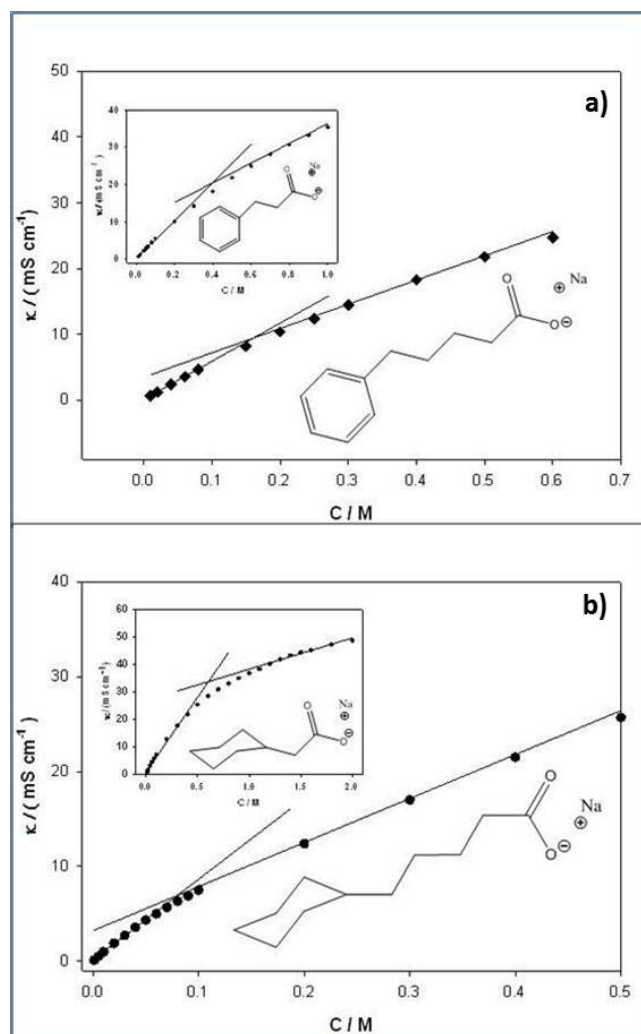


Figure 1. Electrical conductivity profiles of examples of lower and higher homologues of **a)** sodium phenyl-*n*-alkanoates and **b)** sodium cyclohexyl-*n*-alkanoates.

A Klevens type analysis shows two behavioural modes for the phenyl-tipped alkanates. Figure 1a shows that the phenyl-tipped series mirrors the behaviour of the alkylbenzoates, examined in [8]. The break in behaviour seems to occur once more, at four linear carbons. Whereas the aromatic compounds appear to share similarities with each other with respect to the behavioural gradients and breaks, the cyclohexyl-tipped compounds appear different. The *cacs* of the homologues, with the exception of the parent hydrotrope (CyclohexC1), fall on a straight line.

The regular $d\log(cac)/dn \sim 0.285$ is found for most of the homologous series, with the first member being a slight outlier, indicative of the similarity in hydrophobic contribution to the linear carbons by those of the cyclohexyl ring. The equations describing the regions of behaviour are:

C _n Benz	$\log(cac) = -0.2866 n + 0.4179$	6
PhenCx	$\log(cac) = -0.2714 n + 0.5626$	7
CyclohexCx	$\log(cac) = -0.2867 n + 0.0752$	8

These compare well to the Klevens equation (eq. 9.) for regular sodium alkanoates [14], which is gratifying, considering the difficulty in attaining precise *cac* values by conductivity for such compounds, where ionic strength is very high and the *cac* values are large.

linear alkanoates	$\log(cac) = -0.2832 n + 1.5145$	9
-------------------	----------------------------------	---

Skauge and Splitzer [15] investigated CyclohexC1-CyclohexC4 by surface tension, reporting *cac* values in good agreement to those reported here for the higher homologues. Cyclohexanecarboxylate (CyclohexC1) data did not yield a plateau and hence a *cac* for this compound was not reported. Interestingly the *cac* of sodium cyclohexaneacetate (CyclohexC2) was reported having a *cac* of 1 M. This is much higher than the value presented in this study and closer to the *cac* value of the parent hydrotrope reported here. Skauge and Splitzer [15] constructed a Klevens-like equation (eq. 10) by adding all the carbon atoms (ring carbons inclusive) to *n*, which gave a very similar gradient to the sodium alkanoate Klevens equation (eq. 9)

CyclohexCx*	$\log(cac) = -0.29 n + 2.03$	10
-------------	------------------------------	----

As stated previously [8] the difference in intercept values of alkanoates the compounds under study arises from not taking including the hydrophobic effect of the ring moieties into the value of n in the form of n_{eff} . MacInnis *et al.* [16] also investigated these cyclohexane-tipped alkanoates by ^{13}C -NMR and ^{23}Na -NMR reporting *cmc* values in good agreement with those found in [15] and here. They also report a higher *cmc* value for CyclohexC2 at 0.89 M by sodium chemical shift change and 1.02 M by ^{13}C chemical shift change. A more detailed discussion on the discrepancies can found in supporting information.

Examining the hydrophobic contribution of the cyclic components of these compounds (Figure 2b), the benzene ring in both classes reaches limiting values (n_{ring}) of 3-4 when n has reached 4. It is appreciated that the saturated component, cyclohexane, imparts a higher hydrophobic contribution to the structures than the aromatic ring in either case. The stronger hydrophobic contribution of the cyclohexyl group appears constant at $n_{\text{ring}} \sim 5$ and hence higher than the aromatic analogues. The comparison of cyclohexyl to the phenyl ring hydrophobic contribution has been demonstrated recently in branched dodecylammonium bromide analogues containing these ring moieties [17] with the cyclohexyl-tipped compounds possessing a lower *cac* to their phenyl-tipped analogues. As the compared compounds are identical in all structural aspects apart from the ring moieties, then it is reasonable to infer a higher hydrophobic contribution by the cyclohexyl than the phenyl ring.

An interesting point is that the aromatic ring in the parent hydrotrope (sodium benzoate) has a higher hydrophobic contribution than its saturated counterpart (sodium cyclohexanecarboxylate). However when the second behavioural region is reached it appears that the saturated ring has a higher contribution than the aromatic ring, in effect reversing the trend of the first behavioural branch with respect to the ring moiety. Though both governed by the hydrophobic effect, they are thermodynamically different. The break in the aromatic compounds can be seen as occurring due to a switchover in thermodynamic behaviour. In the first behavioural branch it is the aromatic carbons that dominate the aggregation process, switching over to the saturated linear tails in the second branch. The saturated compounds however show no change.

This can be seen to be a result of the small difference between the cyclic saturated carbons and those belonging to the saturated linear tail, which may explain why the parent compounds show such difference in hydrophobic contributions across the three series. Whilst sodium benzoate has a n_{eff} of approximately 6.5 carbon atoms, sodium cyclohexanecarboxylate has a n_{eff} of ~5 carbon atoms. This becomes an interesting point when considering that the *cac* approximately doubles, when the amphiphile ‘acquires’ a double bond [18]. The *cac* values of sodium cyclohexanecarboxylate and sodium benzoate do not compare directly, implying that aromaticity does play a role in promoting aggregation. The possibility of π - π interactions has indeed been suggested in the past [19], however the exact nature of this effect cannot be identified from the results of this study.

The electrical conductivity profiles of all compounds are similar with those of alkylbenzoates [8], in that lower homologues appear to lack clear breaks, whereas the higher homologues show a clear break in gradient. A Kleven's type analysis of the PhenCx series supports the finding of a change in behaviour at four linear carbons in line with the C_nBenz series, which could be seen as the transition point from hydrotropes to surfactants. The CyclohexCx series however reveals that the common Kleven's behaviour, encountered in linear alkanoates, is seen for all cyclohexyl-*n*-alkanoates, whose lower homologues possess *cac* values higher than those of the aromatic series; reinforcing the idea of a hydrophobic, thermodynamic balance at play, between saturated and unsaturated tail carbons.

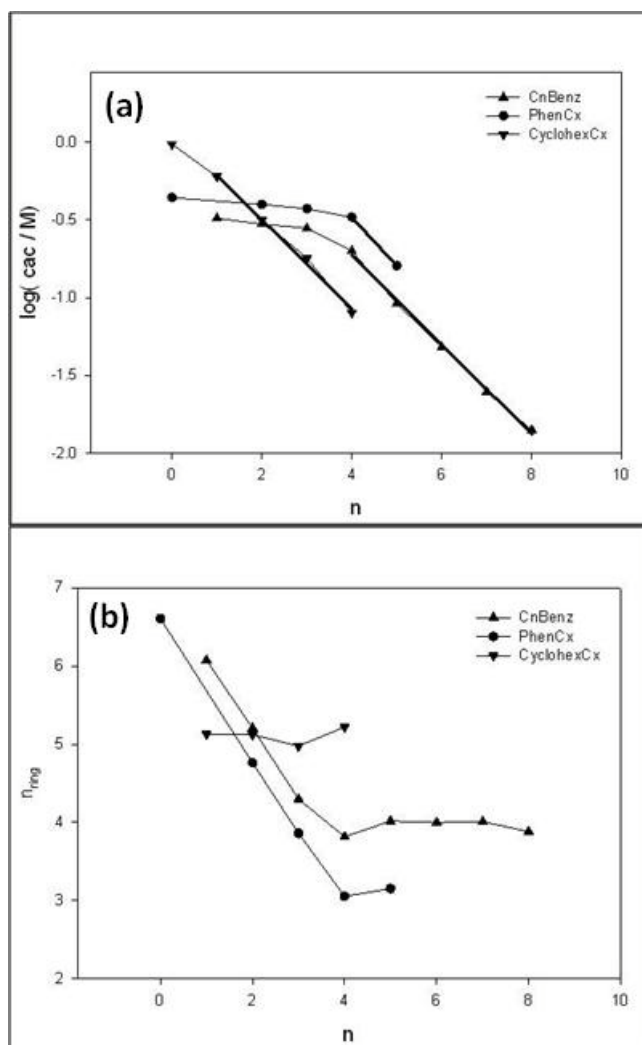


Figure 2. (a) Comparison of behaviour of $\log(\text{cac} / \text{M})$ with hydrophobic chain length (n) for phenyl- n -alkanoates, cyclohexyl- n -alkanoates and n -alkylbenzoates. **(b)** Comparison of hydrophobic contribution of ring moieties (n_{ring}) with hydrophobic chain length (n) phenyl- n -alkanoates, cyclohexyl- n -alkanoates and n -alkylbenzoates. Data for n -alkylbenzoates from [8].

Surface Tension Measurements. All compounds exhibited surface tension behaviour similar to that of common surfactants. Figure 3 illustrates the behaviour surface tension (γ) with activity (a) of PhenCx compounds with the γ -ln(a) plots exhibiting a smooth 'pre-cac' tension decrease followed by a sharp break at the *cac* and a 'post-cac' plateau. Data for PhenC3 were of poor quality, with low reproducibility, but broadly exhibiting similar features to the rest of the homologous series, as was for the carbon number equivalent C2Benz [8]. Despite these difficulties an approximate analysis still yields parameters in accord with the rest of the homologous series (Table 2). CyclohexCx compounds however do not exhibit such inconsistencies (Figure 4) with all compounds behaving like typical surfactants even in the case of the parent hydrotrope sodium cyclohexanecarboxylate with *cac* ~ 1 M. Only two of the PhenCx homologues are presented here due to the presence of impurities in the other compounds, despite being subjected to the same purification method. This can be expected, especially for the lower homologues, as their surface activity is quite low and hence even small amounts of impurities impart a big effect. As such, this is also a testament to the very high purity of the compounds that do exhibit a regular Gibbs isotherm.

For both classes of compounds, the limiting tension γ_{cac} shows a chain length dependence, decreasing with increasing n , consistent with increased alkyl chain density lowering surface energy [20]. The *cac* values as determined by tension measurements are in good agreement with those determined by electrical conductivity (Table 1). A slight decrease in 'pre-cac' gradient with decreasing chain length is seen which was also observed for alkylbenzoates [8]. The pre-cac tensions were analyzed in terms of the Gibbs adsorption equation

$$\Gamma = -\frac{1}{mRT} \frac{d\gamma}{\ln \alpha} \quad 11$$

where Γ is the surface excess (mol m^{-2}), m is a constant associated with ion dissociation (see below), and R and T represent the Gas constant and Temperature. The activity coefficients were estimated using standard procedures [21].

Using a combination of surface tension and neutron reflectivity it has been shown for ionic surfactants ($<10 \text{ mM}$) the prefactor $m = 2$ [22-25] (in the presence of sufficient M^{+2} sequestrant EDTA). This value of $m = 2$ is taken to hold here despite the c_{acs} being much higher than for conventional surfactants. The surface excesses Γ were determined by fitting quadratics to the pre- c_{ac} curves, the function and coefficients were used to generate local tangents and hence Γ vs c profiles. With the coefficients and the associated derivatives used to find the local tangents. Effective head group areas (A_{cac}) were estimated using eq12:

$$A_{cmc} = \frac{1}{\Gamma N_a} \quad 12$$

with N_a the Avogadro number.

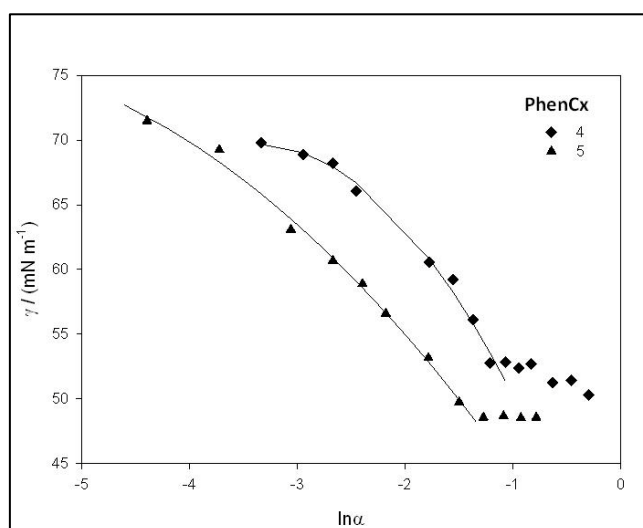


Figure 3. Surface tension (γ) vs $\ln(\alpha)$ of PhenCx homologues. Quadratic equations were fitted to the pre- c_{ac} data, to determine adsorption parameters. Surface tension profiles for other homologues not available due to difficulty in purification.

Table 2. Parameters for PhenCx series, derived from surface tension measurements using the Gibbs equation in terms of activity

PhenCx	activity (α)	$\gamma_{\text{cac}} \pm 0.1$ / (mN m ⁻¹)	$\Gamma_{\text{cac}} \pm 0.1$ / (10 ⁻⁶ mol m ⁻²)	$A_{\text{cac}} \pm 10\%$ / Å ²
4	0.31	52.8	3.1	53.2
5	0.26	48.5	5.0	32.9

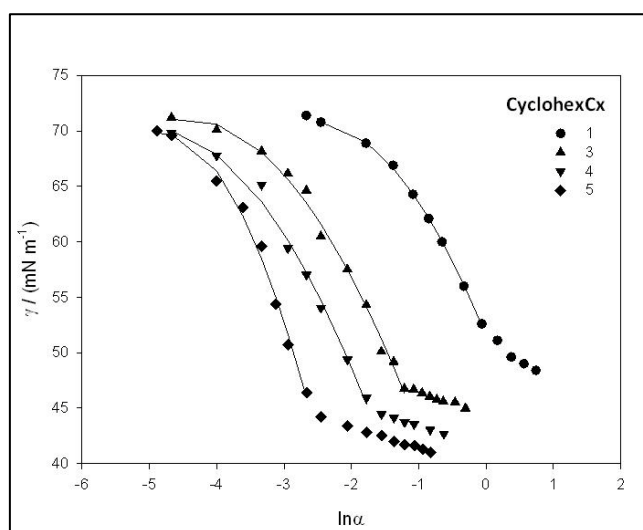


Figure 4. Surface tension (γ) vs $\ln(\alpha)$ of CyclohexCx homologues. Quadratic equations were fitted to the pre-cac data, to determine adsorption parameters.

Table 3. Parameters for the CyclohexCx series, derived from surface tension measurements using the Gibbs equation in terms of activity

CyclohexC _x	activity (α)	$\gamma_{\text{cac}} \pm 0.1$ / (mN m ⁻¹)	$\Gamma_{\text{cac}} \pm 0.1$ / (10 ⁻⁶ mol m ⁻²)	$A_{\text{cac}} \pm 10\%$ / Å ²
1	1.20*	51.1	3.3	50.0
3	0.30	46.8	3.1	53.2
4	0.19	45.0	3.3	50.9
5	0.08	44.0	4.7	34.8

* quoted in C / M

The investigation of CyclohexC1-CyclohexC4 by surface tension by Skauge and Splitzer [15] yielded slightly higher A_{cac} values, at around 60-65 Å², though still comparable to the values ascertained in this study, and with a similar converging trend of values. The discrepancy in A_{cac} values could be attributed to the difference in solution preparation [15], in that the stock solutions were prepared to pH~10, whilst in this study the pH of the solution was not controlled.

The converging limiting adsorption parameters in both PhenCx and CyclohexCx series imply that adsorption is dictated by the ring moieties when the linear tail is short. The higher homologues show lower limiting surface tensions and head group area values, which are more typical of common surfactants. The reduction in γ_{cac} with n follows increased surface chain density [26] longer alkyl chains pack more closely and have lower surface energies.

Pitt et al [20] observed that compounds with similar *cac* values and head group areas but with different tail ends, exhibited limiting surface tensions following the trend of : $\text{CF}_3 < \text{CF}_2 < \text{CH}_3 < \text{CH}_2 < \text{phenyl-}$. Similarly Nave et al. [27] observed that phenyl-tipped Aerosol-OT analogues exhibited higher limiting surface tensions to that of regular CH_3 -tipped Aerosol-OT. These trends hold for this study as well, when analogues of similar *cac* values are compared.

In contrast to conductivity behaviour (Figure 1) there does not appear to be any clear distinction between the air-water adsorption behaviour of the compounds belonging to either behavioural branch of the Klevens plot. The results reveal that difficulties encountered for the lower homologues C_nBenz [8] series are not a result of these compounds possessing physicochemical properties different to common surfactants, and exclusive to 'hydrotropes'; as the CyclohexCx series exhibited well defined behaviour for all homologues, with the lower ones possessing *cac* values considerably higher to the corresponding aromatic analogues. As such surface tension investigations in this study reiterate the conclusion of [8] in that there does not appear to be a behavioural difference between 'hydrotropes' and common surfactants.

A point of interest is that if the surface tension-determined *cac* of CyclohexC1 is used in the Klevens analysis for this series, then all $\log(\textit{cac})$ values fall on the same line (eq. 11) with similar to that obtained by electrical conductivity (eq. 8).

$$\log(\textit{cac}) = -0.2875 n + 0.0776 \quad 13$$

This further emphasizes the thermodynamic similarity of the saturated cyclohexyl-ring carbons to the linear alkane carbons, as well as the difficulty in obtaining precise *cac* values at such low levels of hydrophobicity.

NMR Proton Chemical Shift Measurements. The difference in chemical shifts for the aromatic ring protons between the lowest concentration and those for higher concentrations, defined as $\Delta\delta$ (ppm), was studied as a function of concentration. The behaviour of the shift change with concentration is shown for all PhenCx homologues in Figure 5. The value $\Delta\delta$ is approximately constant in the dilute region, with a change in behaviour at values consistent with the *cac* as determined by electrical conductivity. The change in $\Delta\delta$ behaviour comes from a change in the environment experienced by the protons. Lower homologues appear to go through a smooth transition in behaviour with the $\Delta\delta$ -log(*c*) being curved in the *cac* region. A sharper transition is only observed for the PhenC6 analogue, the highest homologue in the series studied. This $\Delta\delta$ -log(*c*) behaviour was also observed for the *n*-alkylbenzoate series with a definite presence of a clear break point in behaviour appearing at the C5Benz and higher homologues [8]. All PhenCx protons shifted with increasing concentration, which according to the reasoning found in [8] indicates that the phenyl rings are embedded in the aggregates, in accord to the observations made by Martin et al. [17] who employed the more sophisticated ROSEY ^1H NMR experiment to determine the locus of the phenyl- and cyclohexyl-tipped DTAB analogues.

The figure for the behaviour of the shift change of CyclohexCx series protons with concentration can be found in the Supporting information. Again all protons shifted producing a plateau in the dilute region and this time a break in behaviour for all homologues at values consistent with the *cac* values determined by electrical conductivity. A break point is observed for the highest homologue, CyclohexC5, whilst the smaller ones exhibit a smooth transition. Further still all protons shifted in the opposite direction to those of phenyl-*n*-alkanoate protons.

The shift direction to lower ppm values has in the past been attributed to the protons experiencing a more apolar environment [2, 28]. Based on the results of Martin et al. [17], where the cyclohexyl-ring was found to be embedded in the micelle, the parallel of the chemical shift axis to a hydrophobic scale can only be limited to aromatic compounds. It has been previously speculated that the change in direction of the proton chemical shift of the terminal CH₃- protons of surfactants is due to alkyl chain bending towards the aggregate palisade [29, 30].

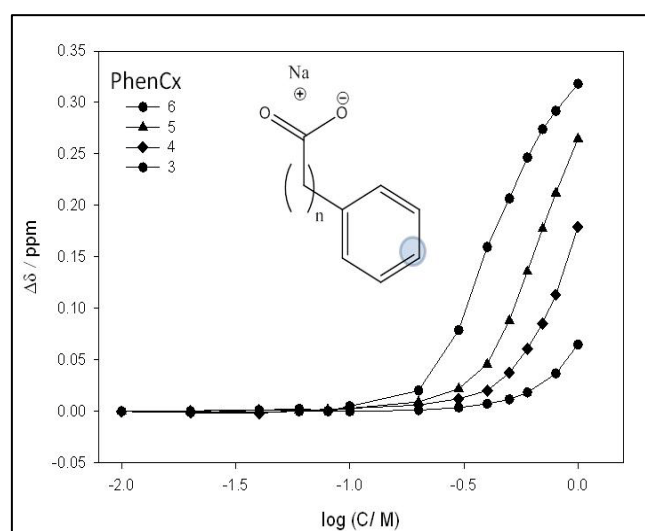


Figure 5. Variation in $\Delta\delta$ / ppm of *para* protons of PhenCx compounds with concentration

With respect to the mode of aggregation these ¹H NMR studies provides an ambiguous picture as due to the existence of a distinction between the smooth transitions of the lower homologues and the sharp breaks observed for the higher homologues.

Small-Angle Neutron Scattering (SANS). SANS is a technique capable of directly probing the nature of amphiphile aggregates and other soft matter, unlike conventional techniques which offer indirect information. By nature of the molecules in this work results will be complementary to the earlier study on *n*-alkylbenzoates [8], which are structurally related.

Hydrotrope solutions in D₂O were prepared as multiples of the *cac* determined from conductivity measurements (Table 1), except for CyclohexC1 where the *cac* was that determined by surface tension. Figure 6 shows example SANS data for PhenC3 and CyclohexC5. With all compounds in this study, the scattering profiles are consistent with charged aggregates, features observed for anionic surfactants like SDS above the *cmc* [31]. The intensity *I*(*Q*) decreases with concentration to the point where it may not be detectable at 1 x *cac* and below. Such behaviour supports a surfactant-like “on-off” mode of aggregation crossing the *cac* (*cmc*), and is observed across the homologous series for both phenyl-*n*-alkanoate and cyclohexyl-*n*-alkanoate classes [see Supporting Information].

Figure 7 shows scattering profiles of PhenCx and CyclohexCx D₂O solutions at 4 x *cac*, showing broadly common behaviour across the series. Increasing chain length leads to increasing *I*(*Q*), with *S*(*Q*) also becoming more pronounced, suggesting stronger aggregate interactions. The data were fitted using the protocol and model described in the Experimental section, being consistent with charged prolate ellipsoidal aggregates at concentrations of 4 x *cac* (Table 2) and 2 x *cac* (Supporting Information).

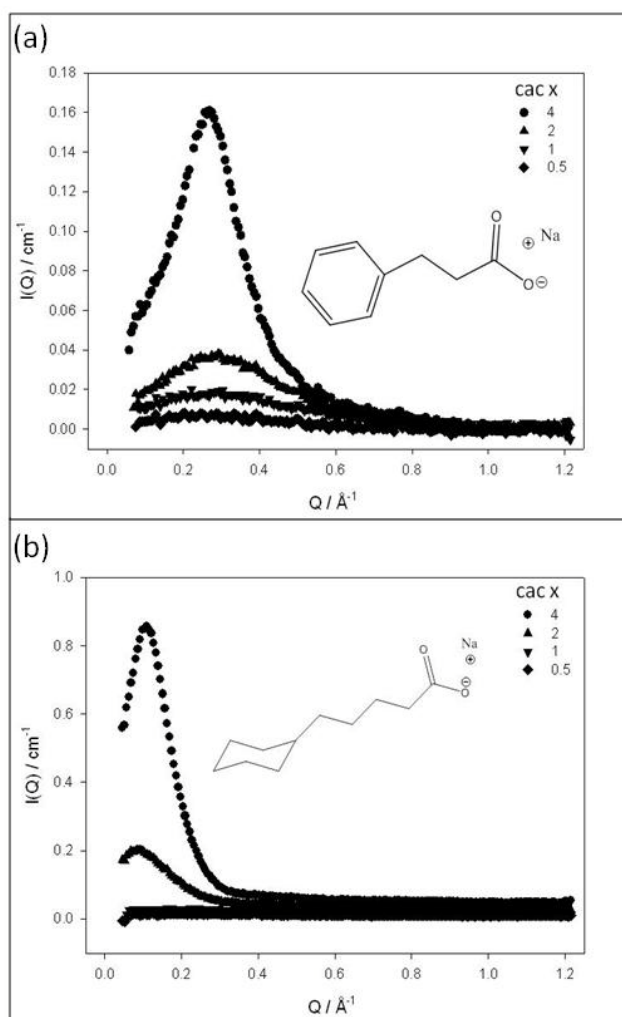


Figure 6. (a) SANS profiles of PhenC3 in D_2O at multiples of the *cac* as determined by electrical conductivity **(b)** SANS profiles of CyclohexC5 in D_2O at multiples of the *cac* as determined by electrical conductivity

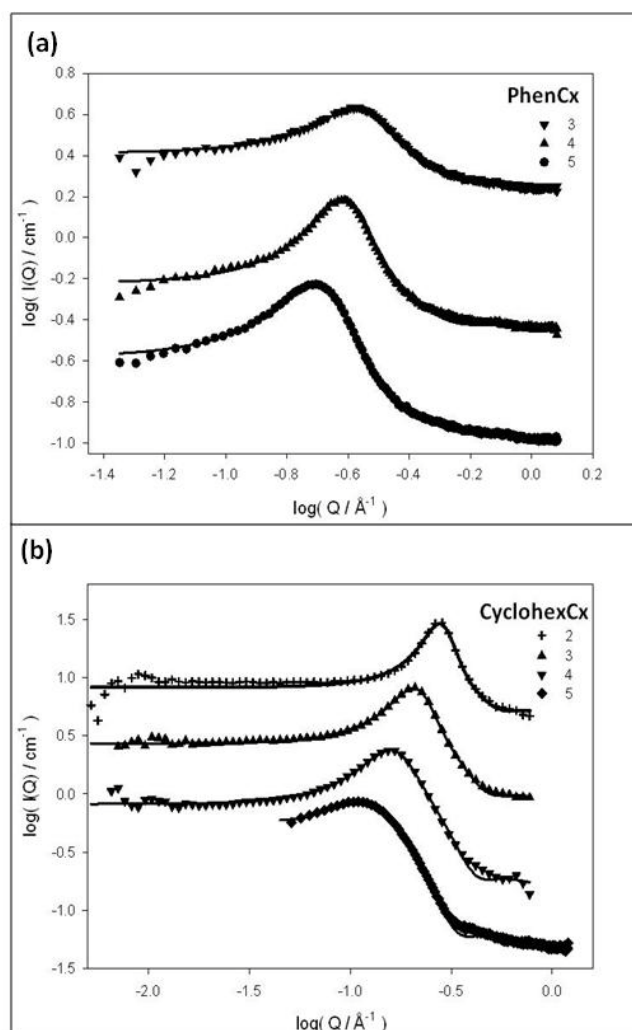
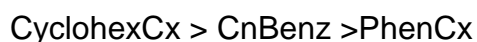


Figure 7. (a) SANS profiles of PhenC3 – PhenC5 in D₂O at 4x cac (PhenC4 offset by +0.8, PhenC3 offset by +1.6) measured on D16 **(b)** SANS profiles of CyclohexCx series in D₂O at 4x cac. (CyclohexC4 offset by +0.5, CyclohexC3 offset by +1, CyclohexC1 offset by +1.5) CyclohexC2-4 measurements were carried out on SANS2d whilst CyclohexC5 was measurements were carried out on D16. Lines are data fits using a charged ellipsoid model described in the text.

The data and analyses show a persistent aggregation behaviour across the homologous series: from the short chain homologues considered ‘true hydrotropes’ to the longer chain homologues, considered closer to ‘true surfactants’, in both saturated cyclohexyl and aromatic phenyl classes.

Comparing the scattering parameters in Table 4 and those reported in [8], it becomes apparent that for equal carbon number molecules aggregates follow the size order:



In the fitting procedure the Tanford equation (eq. 5) was used as a first approximation to the length of the molecules. The aggregate sizes formed for phenyl-*n*-alkanoates were smaller than the predicted molecular length values, and for cyclohexyl-*n*-alkanoates to a lesser extent. For the latter, these discrepancies became smaller with longer molecules.

SANS is a direct report of the presence or absence of (commonly) H-domains in D₂O. Hence its capabilities extend in distinguishing between a gradual step-wise and sharp ‘on-off’ mode of aggregation. The scattering profiles in this study are in line with the previous findings [8]; an ‘on-off’ aggregation mechanism is observed for a further two classes of organic salts. Despite the structural differences between CnBenz, PhenCx and CyclohexCx compounds, which are subtle, though significant, the profiles are consistent with charged ellipsoid structures in all cases. Previous studies by Triolo et al. [6] demonstrated that a wide range of hydrotropes do associate in forms consistent with spherical aggregates near the *cac* and ellipsoid aggregates at higher concentrations. Pal et al. [32] found that sodium butylbenzenesulfonate formed ellipsoid aggregates at approximately eight times the *cac* as determined by Balasubramanian *et al.* [7].

Table 4. Parameters obtained by fitting SANS data to the charged ellipsoid aggregate model for PhenCx and CyclohexCx homologous series at 4 x cac

PhenCx	P(Q)		S(Q)	
	$R_1 / \text{\AA}$	X	$R_{S(Q)}$	$\kappa / \text{\AA}^{-1}$
5	7.9	2.2	10.6	0.221
4	6.7	2.0	8.92	0.403
3	5.0	2.1	8.02	0.771
1*	4.8	1.2	5.5	0.460
CyclohexCx	P(Q)		S(Q)	
	$R_1 / \text{\AA}$	X	$R_{S(Q)}$	$\kappa / \text{\AA}^{-1}$
5	10.1	2.5	15.0	0.186
4	8.9	1.6	11.0	0.268
3	7.8	1.96	8.8	0.375
2	6.9	1.54	9.5	0.731
1**	4.7	2.3	7.94	0.852

* Parameters for C0Benz (sodium benzoate) at 4 x cac taken from [8]

** Parameters for CyclohexC1 (sodium cyclohexanecarboxylate) at 2 x cac

Conclusions

The dilute aqueous phase properties of two classes of cyclic-tipped alkanoates have been investigated, with the results reinforcing the notion that hydrotropes with very different chemical structures exhibit similar solution, interfacial and association properties as common surfactants. These findings support the observations made previously for the linear chain *n*-alkylbenzoate series [8].

Conductivity measurements with both classes of homologues, report a gradual physicochemical change with concentration, which would be consistent with a step-wise aggregation mechanism for the lower homologues, whereas a sharp break in behaviour for higher homologues, more reminiscent of typical surfactant behaviour. Klevens analyses of the chain length dependence of critical aggregation (as in [8]) show that phenyl-*n*-alkanoates exhibit a break in behaviour at four linear carbons, in agreement with other observations with related compounds [7, 8]. Comparing compounds of equivalent carbon number, phenyl-*n*-alkanoates and *n*-alkylbenzoates have broadly similar *cacs*. Interestingly lower homologues of the cyclohexyl-*n*-alkanoate series are more hydrophilic than the equivalent *n*-alkylbenzoates and phenyl-*n*-alkanoates. However, this trend is inverted for higher homologues, with the cyclohexyl-*n*-alkanoates being the most hydrophobic of the three classes. The cyclohexyl-*n*-alkanoates appear to also parallel regular *n*-alkanoates from the first added $-\text{CH}_2-$ onwards, behaviour arising at much shorter chain length than for the aromatic series. These observations reinforce the concept of a thermodynamic balance between ring carbons and linear carbons. Aromatic carbons appear to dominate the aggregation behaviour up to a certain value of *n*, after which the linear $-\text{CH}_2-$ groups take over. Cyclohexyl $-\text{CH}_2-$, being saturated, are closer in nature to the linear tail $-\text{CH}_2-$ carbons, hence the break in behaviour occurs at a much shorter chain length. Surface tension measurements do not exhibit such a distinction in behaviour, with homologues belonging to either $d\log(cac) / dn$ branches of the Klevens plot, exhibiting typical Gibbs adsorption profiles.

NMR experiments are consistent with lower homologues gradually forming ill-defined structures, whereas higher homologues present a more abrupt change more typical of classical surfactants.

SANS profiles on the other hand show clear transitions from apparently non-structured solutions, then giving clear evidence for the presence of aggregates above a certain concentration. As with previous reports on related compounds [6, 8, 31], these additives appear to form ellipsoid-shaped aggregates.

This work reiterates the notion that physicochemical behaviour of 'hydrotropes' is very similar to that of regular surfactants [8]. Further still, amplifying recent work with surfactant ionic liquids (SAILs) [33, 34], it is demonstrated that not all carbons are thermodynamically equal, even though they are hydrophobic enough to drive aggregation and interfacial phenomena. This is now clearly emphasized here, seen in the distinctly different behaviour of saturated cyclic versus aromatic cyclic amphiphiles, as well as for the CH₃/CH₂ groups in surfactant anions and organic counteranions in SAILs [33, 34]. A point not debated often enough is the degree of hydrophobicity of 'unusual' carbons: hence, distinguishing between surfactants and non-surfactant amphiphiles on the basis of hydrophobic moiety atomic arrangements should be revisited. This aspect of surfactant/hydrotrope chemical structure-function relationships deserves further attention for providing a deeper understanding about molecules.

Acknowledgements

The authors would like thank Dr. Craig Butts for useful discussions on NMR. MHH thanks Infineum UK and the EPSRC through the University of Bristol School of Chemistry Doctoral Training Account for the provision of a Ph.D. studentship. We also acknowledge ILL, ISIS and STFC for the allocation of beam time, travel and consumables.

Supporting Information Available

Additional details of hydrotrope solution properties, surface tensions, NMR and neutron scattering data are available free of charge via the Internet at <http://pubs.acs.org>

References

1. Dempsey, G.; Molyneux, P. Solubility of the cosolutes 4-hydroxybenzoic acid and its alkyl esters ('alkylparabens') in aqueous urea: evidence for 1:1 cosolute–urea association in solution and evaluation of the methylene group contribution to the free energy of association. *J. Chem. Soc., Faraday Trans.*, **1992**, 88, 971-977
2. Ferreira, G.; Perigo, D.M.; Politi, M.J.; Schreier, S. Effect of anions from the Hofmeister series and tetracaine to zwitterionic micelles. *Photochem. Photobiol.*, **1996**, 63, 755-761
3. Balasubramanian, D.; Srinivas, V.; Gaikar, V. G.; Sharma, M. M. Aggregation behavior of hydrotropic compounds in aqueous solution. *J. Phys. Chem.* 1989, 93, 3865–3870
4. da Silva, R. C.; Spitzer, M.; da Silva, L. H. M.; Loh, W. Investigations on the mechanism of aqueous solubility increase caused by some hydrotropes. *Thermochim. Acta* **1999**, 328, 161–167
5. Balasubramanian, D.; Srinivas, V.; Rodley, G. A.; Ravikumar, K.; Robinson, W. T.; Turnbull, M. M. Molecular organization in hydrotrope assemblies. *Langmuir*, **1997**, 13, 3235–3239
6. Triolo, R.; Ho, P. C.; Johnson, J. S. Small-Angle Neutron Scattering from Solutions of Low-Equivalent-Weight Organic Salts in D₂O. *J. Phys. Chem.*, **1995**, 99, 9581–9588
7. Balasubramanian, D.; Srinivas, V. When does the switch from hydrotropy to micellar behavior occur. *Langmuir* **1998**, 14, 6658–6661
8. Hopkins Hatzopoulos, M.; Eastoe, J.; Dowding, P.J; Rogers, S.E.; Heenan, R.K.; Dyer, R. 12353 Are hydrotropes distinct from surfactants. *Langmuir* **2011**, 27, 12346-12353
9. Clayden, J., Greeves, N., Warren, S., Wothers, P., *Organic Chemistry*, Oxford University Press, Oxford, 2001
10. Heenan, R. K. *The "FISH" Data Fitting Program Manual*; Rutherford Appleton Laboratory Report RAL-89-129
11. Hayter, J. B.; Penfold, J. An analytic structure factor for maroon solutions. *Mol. Phys.* **1981**, 42, 109–118
12. Tanford, C. *The Hydrophobic Effect*, 2nd ed.; Wiley: New York, 1980

13. Paquette, R. G.; Lingafelter, E. C.; Tartar, H. V. Studies of sulfonates VII. Conductances and densities of sodium ethyl-, n-butyl-, n-octyl-, and n-dodecylbenzene-p-sulfonate solutions. *J. Am. Chem. Soc.* **1943**, 65, 686–692
14. Klevens, H. B. Critical micelle concentrations as determined by refraction. *J. Phys. Colloid Chem.* **1948**, 52, 130–148
15. Skauge, A.; Splitzer, J. Surface tensions and micellization of omega - cyclohexylalkanoic acids and their sodium salts. *J. Phys. Chem.*, **1983**, 87, 2398-2401
16. MacInnis, J.A; Palepu, R.; Marangoni, G. NMR Investigations of the micellar properties of the sodium salts of cyclohexylalkanoic acids. *Can J. Chem.* **1999**, 77, 1994-2000
17. Martin, V.I.; Rodriguez, A.; del Mar Graciani, M.; Robina, I.; Carmona, A.; Moyá, M.L. Physicochemical characterization of bromide mono- and dimeric surfactants with phenyl and cyclohexyl rings in the head group. *J. Colloid Interface Sci.*, **2011**, 363, 284-294
18. Shinoda, K.; Nakagawa, T.; Tamamushi, B.; Isemura, T. *Colloidal Surfactants*; Academic Press: New York and London, 1963
19. Eastoe, J.; Hopkins Hatzopoulos, M.; Dowding, P.J. Action of hydrotropes and alkyl-hydrotropes. *Soft Matter* **2011**, 7, 5917-5925
20. Pitt, A. R.; Morsley, S. D.; Burbridge, N. J.; Quickenden, E. L. The relationship between surfactant structure and limiting values of surface tension, in aqueous gelatin solution, with particular regard to multilayer coating. *Colloids Surf., A.* **1996**, 114, 321–335
21. Atkins, P.; de Paula, J. *Atkins Physical Chemistry*, 7th ed.; Oxford University Press: New York, 2002
22. Eastoe, J.; Downer, A.; Pitt, A. R.; Simister, A.; Penfold, J. Effects of hydrophobic chain structure on adsorption of fluorocarbon surfactants with either CF₃- or H-CF₂-terminal groups. *Langmuir* **1999**, 15, 7591–7599
23. Eastoe, J.; Mohamed, A.; Trickett, K.; Chin, S. W.; Cummings, S.; Sagisaka, M.; Hudson, L.; Nave, S.; Dyer, R.; Rogers, S. E.; Heenan, R. K. Universal Surfactant for Water, Oils, and CO₂. *Langmuir* **2010**, 26, 13861–13866
24. Nave, S.; Eastoe, J.; Penfold, J. What is so special about Aerosol-OT? 1. Aqueous systems. *Langmuir* **2000**, 16, 8733–8740

25. Li, Z. X.; Lu, J. R.; Thomas, R. K. Neutron reflectivity studies of the adsorption of Aerosol-OT at the air/water interface: The surface excess. *Langmuir* **1997**, 13, 3681–3685
26. Rosen, M. J. *Surfactants and Interfacial Phenomena*, 2nd ed.; Wiley: New York, 1989
27. Nave, S.; Paul, A.; Eastoe, J.; Pitt, A.; Heenan, R. What is so special about Aerosol-OT? Part IV. Phenyl-tipped surfactants. *Langmuir*, **2005**, 21, 22, 10021-10027
28. Das, S.; Bhirud, R.G.; Nayyar, N.; Narayan, K.S.; Kumar, V.V. Chemical-shift changes on micellisation of linear alkylbenzenesulfonate and oleate. *J. Phys. Chem.* **1992**, 96, 7454-7457
29. Balasubramanian, D.; Shobha, J. Hairpin looping of terminally functionalized carboxylate surfactants. *J. Phys. Chem.* **1986**, 90, 2800-2802
30. Gruen, D.W.R. A model for the chains in amphiphilic aggregates. 2. Thermodynamic and experimental comparisons for aggregates of different shape and size. *J. Phys. Chem.* **1985**, 89, 146, 153-163
31. Bezzobotov, V. Y.; Borbely, S.; Cser, L.; Farago, B.; Gladkih, I. A.; Ostanevich, Y. M.; Vass, Sz. Temperature and concentration dependence of properties of sodium dodecylsulfate micelles determined from small-angle neutron scattering. *J. Phys. Chem.* **1988**, 92, 5738–5743
32. Pal, O. P.; Gaikar, V. G.; Joshi, J. V.; Goyal, P. S.; Aswal, V. K. Small-angle neutron scattering studies of sodium butylbenzenesulfonate aggregates in aqueous solution. *Pramana* **2004**, 63, 357–362
33. Brown, P.; Butts, C.; Dyer, R.; Eastoe, J.; Grillo, I.; Guittard, F.; Heenan, R.; Rogers, S. Anionic surfactants and surfactant ionic liquids with quaternary ammonium counterions. *Langmuir* **2011**, 27, 4563-4571
34. Brown, P.; Butts, C.; Eastoe, J.; Fermin, D.; Grillo, I.; Lee, H-G.; Parker, D.; Plana, D.; Richardson, R. Anionic surfactant ionic liquids with 1-butyl-3-methyl-imidazolium cations: Characterization and application. *Langmuir* **2012**, 28, 5, 2502-2509